

## REMARKS

### A. Status of the Claims

Claims 1 and 11-26 are pending in this application. Claims 1 and 26 are amended to more particularly point out and distinctly claim the invention; claims 12-15 and 19-21 are withdrawn as directed to a nonelected species; and claims 1, 11, 16-18 and 22-26 were examined in the February 7, 2008 Office Action.

### B. Rejections under 35 U.S.C. 103(a)

Claims 1, 11, 16-18 and 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Capon et al., U.S. Patent Application Publication US 2002/0034732 and Olivo et al., Virology 251:198-205 (1998). The Office Action states that Capon et al. discloses a method for determining the susceptibility for an HCV antiviral drug or HCMV antiviral drug comprising the steps of a) introducing a resistance test vector comprising a patient-derived segment and an indicator gene into a host cell; b) culturing the host cell; c) measuring the expression of the indicator gene in a target host cell; and d) comparing the expression of the indicator gene either in the presence or absence of an antiviral drug. Olivo et al. is cited for stating that preparing a replicon cell culture is simple. The PTO acknowledges that neither reference discloses, among other features, combining two cell cultures each containing a distinct subgenomic viral replication system. However, the PTO asserts that “it would have been obvious for the ordinary artisan to screen for antiviral effects of a single drug on cell cultures containing cells infected with multiple subgenomic viral replication systems. One would have been motivated to do so in order to efficiently determine the antiviral activity of a single drug for multiple subgenomic viral replication systems at once.” Applicants request reconsideration and withdrawal of this rejection in light of the following discussion.

In order to sustain a rejection under 35 U.S.C. 103(a), the cited references must, alone or in combination, recite every element in the claims. While the Office Action acknowledges that neither reference discloses combining two cell cultures where each contains a distinct subgenomic viral replication system, it asserts that the combining of the two cell cultures is nonetheless obvious because there was motivation to combine the cell cultures, based on the benefits realized by doing so. However, to base an obviousness reference on a modification of a reference simply because of the benefits realized, where the modification was not taught or

suggested in the cited art, "...office personnel must resolve the Graham factual inquiries. Then, Office personnel must articulate the following:

(1) a finding that there was some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;

(2) a finding that there was reasonable expectation of success; and

(3) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness."

MPEP 2143.

Thus, to sustain a rejection under 103(a) when there is no reference that teaches or even suggests that two cell cultures comprising subgenomic viral replication systems be combined, there must be knowledge for combining the cell cultures generally available to one of ordinary skill in the art. However, since the PTO could find no reference where cell cultures comprising subgenomic viral replication systems are combined, it is clear that such knowledge was not generally available to the skilled artisan. Thus, the PTO practiced impermissible hindsight to find that combining the two cell cultures would be obvious, since there was no other indication that knowledge for combining the cell cultures that is generally available. Additionally, even though this analysis requires a Graham factual inquiry, the Office Action provides no such analysis.

Since there is no teaching or suggestion in the prior art that two cell cultures comprising subgenomic viral replication systems be combined, and since there is also no knowledge available to the skilled artisan for combining two cell cultures, Applicants assert that the rejection under 35 U.S.C. 103(a) cannot be sustained. Accordingly, withdrawal of the rejection is respectfully requested.

## CONCLUSION

In light of the above discussion, applicants respectfully request withdrawal of all rejections, passage of the examined claims 1, 11, 16-18 and 22-26 to allowance, and examination of withdrawn claims 11-15 and 19-21, which all depend from claim 1.

Respectfully submitted,

/Elie H. Gendloff/

Elie H. Gendloff  
Reg. No. 44,704  
Attorney for Applicants

Sonnenschein Nath & Rosenthal LLP  
Post Office Box 061080  
Wacker Drive Station, Sears Tower  
Chicago IL 60606-1080  
Tel.: 212-768-6926  
Fax: 212-768-6800

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